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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/909,574	07/20/2001	Frank A. Skraly	MBX 039	2982

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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 04/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/909,574	SKRALY ET AL.	
	Examiner	Art Unit	
	Yong D. Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on February 2, 2005, amending claims 1, 8 and 10, has been entered.

Claims 1-4 and 6-10 are pending.

Response to Arguments

Applicant's arguments filed on February 2, 2005 have been fully considered but they are not persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4, 6-8 and 10 are rejected under 35 U.S.C. 101 because the claimed invention is directed to a non-statutory subject matter.

Claims 1-4, 6-8 and 10 are drawn to a method of using an organism, which encompasses human beings. Claims drawn to a method of using humans are considered non-statutory subject matter. MPEP 2105 states that if the broadest reasonable interpretation of the claimed invention as a whole encompasses a human being, then the claimed invention is directed to nonstatutory subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 recite the phrase "genes". The metes and bounds of the phrase in the context of the above claim is not clear to the Examiner. A perusal of the specification did not provide the Examiner with a specific definition for the above phrase.

In response to the previous Office Action, applicants have traversed the above rejection. Applicants argue that claim 8 has been amended to recite that the organism expresses the "genes". The metes and bounds of the phrase in the context of the above claim is not clear to the Examiner. A "gene" is generally understood in the art as comprising a coding sequence, introns, exons and regulatory sequences. A perusal of the specification did not provide the Examiner with a specific definition for the above term. Therefore, it is not clear whether the above term in said claims encompass the intronic and regulatory sequences or is limited to a cDNA. Examiner suggests replacing the above term with "polynucleotide".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 and 6-10 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-4 and 6-10 are drawn to a method for producing polyhydroxyalkanoates from 4-hydroxybutyrate, 2-hydroxybutyrate, 4-hydroxyvalerate, 5-hycroxyvalerage, 6-hydroxyhesanoate, 2-hydroxyethannoate, 2-hydroxypriopionate and 3-hydroxyhexanoate in any organism, wherein the hydroxyalkanoates are produced from any diols using any diol oxidoreductase and any aldehyde dehydrogenase which are active in bacteria and plants. Although claims 2-4 and 6-7 are limited to specific diols, the hydroxyalkanoates are produced using any diol oxidoreductase and any aldehyde dehydrogenase which are active in bacteria or plants. Therefore, these claims are drawn to a method of using a genus of diol oxidoreductase having any structure which are active in bacteria or plants, a genus of aldehyde dehydrogenase having any structures which are active in bacteria or plants, a genus of organisms and/or a genus of any diols. The genus of diol oxidoreductase and the genus of aldehyde dehydrogenase comprise of numerous enzymes that may or may not convert 1,6-hexanediol, 1,5-pentaediol, 1,4-butanediol, 1,3-propanediol, 1,2-ethanediol and 1,2-propanediol to its corresponding hydroxyalkanoate. And, a genus of diol oxidoreductase and genus of aldehyde dehydrogenase comprise of numerous enzymes that may or may not convert any diols to 4-hydroxybutyrate, 2-hydroxybutyrate, 4-hydroxyvalerate, 5-hycroxyvalerage, 6-hydroxyhesanoate, 2-hydroxyethannoate, 2-

hydroxypriopionate and 3-hydroxyhexanoate. And, any organism, i.e. mammals, may or may not be able to form polyhydroxyalkanoates even if all enzymes recited in the claims are present.

Further, the genus comprising aldehyde dehydrogenase comprise of species that are structurally unrelated and utilize substrates unrelated to the diols listed above (see ExPASy database: aldehyde dehydrogenase). Similarly, the genus comprising diol oxidoreductase comprises of species that are structurally unrelated and utilize substrates unrelated to the diols listed above (See ExPASy database: diol oxidoreductase). The specification only describes a method of producing polyhydroxyalkanoates from hydroxyalkanoates by converting 1,6-hexanediol, 1,5-pentaediol, 1,4-butanediol, 1,3-propanediol, 1,2-ethanediol or 1,2-propanediol in bacteria with an aldehyde dehydrogenase (aldH) from *E. coli* and a 1,3-propanediol oxidoreductase (dhaT) from *K. pneumoniae*. Therefore, the specification fails to describe a representative species of the genus of diol oxidoreductase, genus of aldehyde dehydrogenase, genus of diols and genus of organism that are able, in combination, to convert diols to said hydroxyalkanoates.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 1-4 and 6-10.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that since the claims have been amended to recite diol oxidoreductase and aldehyde dehydrogenase which are active in bacteria or plants, the claims are no longer drawn to diol oxidoreductase or aldehyde dehydrogenase having any structure. Examiner respectfully disagrees. While it is true that the claims are now drawn to a method of using diol oxidoreductase and aldehyde dehydrogenase which are active in bacteria or plants, the claims remain drawn to a method of using a genus of diol oxidoreductase and aldehyde dehydrogenase which are active in bacteria or plants. Further, it is unclear how this new limitation describes the structure of the enzymes.

Applicants also argue that diol oxidoreductase and aldehyde dehydrogenase were well known in the art. Even though some members of the genus of diol oxidoreductase and genus of aldehyde dehydrogenase were known in the art, neither art or the specification describes a method of producing polyhydroxyalkanoates in any organism using any diol oxidoreductase and aldehyde dehydrogenase which are active in bacteria and plants by converting any diols into the recited hydroxyalkanoate monomers. Also, the references of Luers et al. and Tong et al. cited by applicants describe a method of using diol oxidoreductase to produce 1,3-propanediol.

Applicants also argue that many different organisms have the cellular machinery to produce polyhydroxyalkanoates. Examiner respectfully disagrees. Production of polyhydroxyalkanoates are known in microorganism, neither art nor specification

describes a method of producing polyhydroxyalkanoates in any organism, including animals. Also, production of polyhydroxyalkanoates in plants is limited. Art teaches that production of polyhydroxyalkanoates in plants is complicated because metabolism in plants is compartmentalized (Huisman et al. – form PTO-1449).

Applicants also argue that the claims are not directed to any diols but to diols which lead to the production of specific hydroxyalkanoates. Examiner respectfully disagrees. The claims do not recite a limitation to the type of diols employed in the method.

Claims 1-4 and 6-10 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing polyhydroxyalkanoates from hydroxyalkanoates in bacteria by converting 1,6-hexanediol, 1,5-pentaediol, 1,4-butanediol, 1,3-propanediol, 1,2-ethanediol or 1,2-propanediol to its corresponding hydroxyalkanote using an aldehyde dehydrogenase (aldH) from *E. coli* and a 1,3-propanediol oxidoreductase (dhaT) from *K. pneumoniae,* does not reasonably provide enablement for a method of producing polyhydroxyalkanoates from hydroxyalkanoates using any or all diol oxidoreductases, any or all aldehyde dehydrogenases in any organism by converting any diols to hydroxyalkanoates. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 1 and 8-10 are drawn to a method for producing polyhydroxyalkanoates from 4-hydroxybutyrate, 2-hydroxybutyrate, 4-hydroxyvalerate, 5-hycroxyvalerage, 6-hydroxyhesanoate, 2-hydroxyethannoate, 2-hydroxypriopionate and 3-hydroxyhexanoate in any organisms wherein the hydroxyalkanoates are produced by converting any diols to said hydroxyalkanoates with any diol oxidoreductase and any aldehyde dehydrogenase. While claim 2 through 7 limit the diols used in the method, said claims continue to encompass the use of any or all aldehyde dehydrogenases which are active in bacteria or plants, diol oxidoreductases which are active in bacteria or plants and any organism.

Many different oxidoreductase from the family of diol dehydrogenase are known and many different dehydrogenase from the family of aldehyde dehydrogenases are known (see ExPASY database: aldehyde dehydrogenase and ExPASY database: diol oxidoreductase). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of diol

dehydrogenase, aldehyde dehydrogenase and diols broadly encompassed by the claims.

It would require undue experimentation of the skilled artisan to make and use the claimed method to convert any diols into 4-hydroxybutyrate, 2-hydroxybutyrate, 4-hydroxyvalerate, 5-hycroxyvalerage, 6-hydroxyhesanoate, 2-hydroxyethannoate, 2-hydroxypriopionate and 3-hydroxyhexanoate using any diol oxidoreductase and any aldehyde dehydrogenase. It would also require undue experimentation of the skilled artisan to make and use the claimed method to convert 1,6-hexanediol, 1,5-pentaediol, 1,4-butanediol, 1,3-propanediol, 1,2-ethanediol or 1,2-propanediol into 4-hydroxybutyrate, 2-hydroxybutyrate, 4-hydroxyvalerate, 5-hycroxyvalerage, 6-hydroxyhesanoate, 2-hydroxyethannoate, 2-hydroxypriopionate or 3-hydroxyhexanoate using any diol oxidoreductase and aldehyde dehydrogenase. The specification is limited to teaching the use of an aldehyde dehydrogenase (aldH) from *E. coli* and a 1,3-propanediol oxidoreductase (dhaT) from *K. pneumoniae* to produce 4-hydroxybutyrate, 2-hydroxybutyrate, 4-hydroxyvalerate, 5-hycroxyvalerage, 6-hydroxyhesanoate, 2-hydroxyethannoate, 2-hydroxypriopionate and 3-hydroxyhexanoate from 1,6-hexanediol, 1,5-pentaediol, 1,4-butanediol, 1,3-propanediol, 1,2-ethanediol or 1,2-propanediol but provides no guidance with regard to the making of said hydroxyalkanoates with any diols and any diol oxidoreductase and any aldehyde dehydrogenase. The specification also does not provide guidance with regarding to the making of said hydroxyalkanoates with any diol oxidoreductase and any aldehyde dehydrogenase.

In view of the great breadth of the claim, amount of experimentation required to make the claimed hydroxyalkanote, the lack of guidance, working examples, and unpredictability of the art in predicting which diol oxidoreductase, aldehyde dehydrogenase, organism and/or diol to use, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the method encompassed by the claims.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including method of making hydroxyalkanoates derived from any diols using any diol oxidoreductase and any aldehyde dehdyrogenase and a method of making hydroxyalkanoates derived from 1,6-hexanediol, 1,5-pentaediol, 1,4-butanediol, 1,3-propanediol, 1,2-ethanediol or 1,2-propanediol using any diol oxidoreductase and any aldehyde dehdyrogenase. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of which diol oxidoreductase, aldehyde dehydrogease, organsim and/or diols to use is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that the specification and the prior art discloses organisms that can be used to produce polyhydroxyalkanoates, diols that may be utilized to form the claimed polyhydroxyalkanoate monomers and diol oxidoreductases and aldehyde dehydrogenases used to convert diols into hydroxyalkanoate monomers. Examiner respectfully disagrees, as discussed above.

Applicants also argue that applicants have two issued patents with claims directed to the production of polyhydroxyalkanoates by providing diols to genetically engineered organisms. As applicants note, claims in these issued patents are not directed to the claimed subject matter of the instant invention and applicants' arguments are moot.

Applicants also argue that there is no requirement for examples and applicants have provided numerous working examples and requires only routine experimentation. Examiner respectfully disagrees. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of diol dehydrogenase, aldehyde dehydrogenase, diols and organisms broadly encompassed by the claims. It would require undue experimentation of the skilled artisan to make and use the claimed method to convert any diols into the recited hydroxyalkanoate monomers using any diol oxidoreductase and any aldehyde dehydrogenase in any organism. In view of the great breadth of the claim, amount of experimentation required to make the claimed hydroxyalkanote, the lack of guidance, working examples, and unpredictability of the art in predicting which diol oxidoreductase, aldehyde

dehydrogenase, organism and/or diol to use, the claimed invention would require undue experimentation.

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner 1652

Manjunath Rao
Primary Examiner 1652